

## Complete Summary

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### GUIDELINE TITLE

Lipids.

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Lipids. Singapore: Singapore Ministry of Health; 2001 Jul. 52 p. [19 references]

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Dyslipidaemia

### GUIDELINE CATEGORY

Evaluation  
Prevention  
Treatment

### CLINICAL SPECIALTY

Cardiology  
Endocrinology  
Family Practice  
Internal Medicine  
Nutrition

### INTENDED USERS

Advanced Practice Nurses  
Nurses  
Physician Assistants  
Physicians

## GUIDELINE OBJECTIVE(S)

To assist physicians and other health care professionals in clinical decision making providing well-balanced information on the management of patients with dyslipidaemia, without restricting the physician's individual clinical judgment

## TARGET POPULATION

Patients at risk for or with dyslipidaemia

## INTERVENTIONS AND PRACTICES CONSIDERED

### Evaluation

1. Laboratory measurements including total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG)
2. Assessment of risk based on laboratory measurements, presence of coronary heart disease (CHD), or other atherosclerotic disease, and identification of major risk factors including cigarette smoking, hypertension, low high-density lipoprotein cholesterol, family history of premature coronary heart disease, and age

### Prevention

1. Population- and individually-based primary prevention strategies including mass education of the public and identification of high risk patients

### Treatment

1. Lifestyle changes such as cessation of cigarette smoking, diet, and exercise
2. Drug therapy with fibrates, statins, nicotinic acid, omega 3 fish oils, and combination therapy

## MAJOR OUTCOMES CONSIDERED

- Coronary heart disease (CHD)
- Cerebrovascular events
- Morbidity and mortality due to coronary heart disease
- Total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride levels

## METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

American College of Cardiology/American Heart Association ranking for level of evidence:

- A. Data derived from multiple randomized clinical trials involving large numbers of individuals.
- B. Data derived from a limited number of trials involving comparatively small numbers of patients or from well-conceived data analyses of nonrandomized studies or observational data registries.
- C. Consensus opinion of experts was the primary source of recommendation.

#### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

#### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

American College of Cardiology/American Heart Association ranking for level of evidence for classification of recommendations for a diagnostic procedure, a particular therapy, or an intervention:

I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful and effective

II: Conditions for which there is conflict of evidence and/or a divergence of opinion about usefulness/efficacy of procedure or treatment

II a: Weight of evidence/opinion is in favour by evidence/efficacy

II b: Usefulness/efficacy is less well established by evidence/opinion

III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

An outline of the provisional guidelines was presented at the 1999 Singapore Cardiac Society Annual Scientific Meeting. Subsequently, these guidelines were further modified and elaborated upon by the workgroup.

# RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

Each recommendation is rated based on the level of the evidence and the classes of the recommendation. Definitions of the levels of the evidence (A, B, C) and classes of the recommendations (Level I through Level III) are presented at the end of the "Major Recommendations" field.

### Laboratory Lipid Measurements

Who should be tested?

A lipid profile consisting of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) should be obtained in the following individuals:

- I: Patients with coronary heart disease, cerebrovascular or peripheral artery disease  
Class I, Level A
- I: Diabetic patients  
Class I, Level A
- I: Individuals with a family history or clinical evidence of familial hyperlipidaemia  
Class I, Level A
- I: Individuals with other risk factors for coronary heart disease  
Class I, Level B

It is also reasonable to test individuals who are undergoing a general health screening.

Serum total cholesterol and high-density lipoprotein cholesterol levels can be measured at any time of the day in the non-fasting state. However, triglyceride levels must be obtained after 10 to 12 hours of fasting. Total cholesterol, high-density lipoprotein cholesterol and triglycerides are measured directly. Low-density lipoprotein cholesterol is usually calculated using the Friedwald formula:  $LDL-C \text{ (mmol/L)} = TC - (HDL-C + TG/2.2)$ . This formula cannot be used if the triglyceride level is greater than or equal to 4.5 mmol/L (400 mg/dL). Direct measurement of low-density lipoprotein cholesterol is now available in certain laboratories in Singapore.

What are the precautions to be taken?

- 10 to 12 hours of fasting is necessary for the estimate of triglycerides
- The individual's posture should be consistent, i.e., either always sitting (usual practice) or always lying
- Defer tests for at least 2 weeks after a febrile illness
- For patients suffering from acute myocardial infarction, the cholesterol level may be depressed between 24 hours to about 3 months after the infarction
- Since cholesterol and triglyceride levels show biological variability, it is advisable to obtain at least 2 consecutive estimations (1 to 8 weeks apart) before deciding on any therapeutic intervention

### Risk Assessment - First Step in Risk Management

Assessment of risk status

I: In the management of dyslipidaemia, a global approach consisting of an assessment and management of all risk factors is essential. Risk stratification is also important and priorities for treatment should be given to those individuals who are at the highest risk (e.g., patients with pre-existing coronary heart disease or coronary heart disease risk equivalents\*).

Class I, Level A

Note: See the original guideline document for a discussion of risk assessment.

### Goal Lipid Levels and the Levels for Initiating Drug Therapy

IIa: It is important to note that the higher the risk category, the lower will be the goal low-density lipoprotein cholesterol level and the level for initiating drug therapy.

Class IIa, Level B

Target cholesterol levels

IIa: Patients with coronary heart disease or coronary heart disease risk equivalents\*: Total cholesterol <4.1 mmol/L (160 mg/dl), low-density lipoprotein cholesterol <2.6 mmol/L (100 mg/dl).

Class IIa, Level B

IIa: Individuals without coronary heart disease or coronary heart disease risk equivalents\*, but who have  $\geq 2$  risk factors: total cholesterol  $< 5.2$  mmol/L (200 mg/dl), low-density lipoprotein cholesterol  $< 3.4$  mmol/L (130 mg/dl).  
Class IIa, Level B

IIa: Individuals without coronary heart disease or coronary heart disease risk equivalents\* and who have 0 to 1 risk factor: total cholesterol  $< 6.2$  mmol/L (240 mg/dL), low-density lipoprotein cholesterol  $< 4.1$  mmol/L (160 mg/dl). Lower levels down to total cholesterol  $< 5.2$  mmol/L (200 mg/dL) or low-density lipoprotein cholesterol  $< 3.4$  mmol/L (130 mg/dL) are desirable if these can be achieved with lifestyle changes alone.  
Class IIa, Level B

IIa: For the Singapore population in general, the recommended target cholesterol levels are: total cholesterol  $< 5.2$  mmol/L (200 mg/dl), low-density lipoprotein cholesterol  $< 3.4$  mmol/L (130 mg/dL).  
Class IIa, Level B

\*Coronary heart disease risk equivalents = cerebrovascular disease, peripheral artery disease or diabetes mellitus.

### Lifestyle Changes

I: Lifestyle changes are an integral part of overall management. They are the mainstay in population based primary prevention strategies. Their major advantages are:

- An absence of side-effects which may sometimes occur with drug therapy and
- Minimal costs

Class I, Level A

Cigarette smoking. Cigarette smoking should be stopped immediately.

Weight reduction. Weight reduction is achieved mainly by dietary therapy and exercise.

Dietary. To lower total cholesterol and low-density lipoprotein cholesterol: (1) reduce intake of total fat, saturated fat and total cholesterol, and (2) increase the proportion of monounsaturated and polyunsaturated fat (see Annex 1 titled "Dietary Therapy of Hypercholesterolemia" in the original guideline document). In addition, to lower triglyceride levels, it is necessary to reduce total calorie, carbohydrate and alcohol intake.

Exercise. Aerobic exercise such as brisk walking, jogging, swimming and cycling are recommended 3 to 4 times per week. Each exercise session should be about 30 to 40 minutes (National Institutes of Health [NIH] Consensus Panel, 1996; Lee, 2000). Less strenuous exercise has also been shown to be beneficial and is recommended in individuals who cannot exercise vigorously.

Alcohol restriction. Alcohol intake should be restricted in individuals with hypertriglyceridaemia.

Assessing response to lifestyle changes. Repeat lipid profile 3 months after lifestyle changes have been initiated to assess response.

### Drug Therapy

What are the recommended drugs for hypercholesterolemia?

I: HMG-CoA reductase inhibitors (statins) are the preferred drugs followed by the resins.

Class I, Level A

What are the recommended drugs for hypertriglyceridaemia?

I: Fibrates are the drugs of choice in the treatment of hypertriglyceridaemia (Fruchart, Brewer, & Leitersdorf, 1998; Frick et al, 1987).

Class I, Level A

What are the recommended drugs for mixed dyslipidaemia?

IIa: Start first with:

- A statin if the predominant lipid abnormality is an elevated low-density lipoprotein cholesterol. If the triglyceride level remains unacceptably high despite the statin, consider adding a fibrate.
- A fibrate if the predominant lipid abnormality is hypertriglyceridaemia. If the low-density lipoprotein cholesterol remains unacceptably high despite the fibrate, consider adding a statin.

Class IIa, Level B

The decision to combine a statin and a fibrate must be individualized and should be initiated only when it is strongly indicated.

How should isolated low high-density lipoprotein cholesterol be treated?

IIa: Based on the results of the recent U.S. Veterans Affairs High-density Lipoprotein Cholesterol Intervention Trial (VA-HIT) (Rubins HB, Robins SJ, Collins D, et al. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. N Eng J Med 1999; 341:410-8), coronary heart disease patients whose primary lipid abnormality is a low high-density lipoprotein cholesterol despite lifestyle changes can be given fibrate to elevate the high-density lipoprotein cholesterol level (Rubins et al, 1999).

Class IIa, Level B

How long should drug therapy be continued?

IIa: Most patients require medication for life, especially patients with familial hyperlipidaemias. In dyslipidaemia secondary to diet and lifestyle indiscretion, it may be possible to discontinue drug therapy when goal levels have been reached. However, the lipid levels should be monitored carefully 3 to 4 months after stopping treatment.

Class IIa, Level C

When should patients be referred to a specialist?

IIa: Patients who remain outside the target values despite adequate dietary and maximal drug therapy should be referred to lipid specialists.

Class IIa, Level C

### Special Considerations

See the original guideline document regarding the following special considerations:

- Diabetes mellitus
- Children
- Women
- Pregnancy
- Elderly
- Renal disease
- Liver disease

### Definitions:

Levels of Evidence:

- A. Data derived from multiple randomized clinical trials involving large numbers of individuals.
- B. Data derived from a limited number of trials involving comparatively small numbers of patients or from well-conceived data analyses of nonrandomized studies or observational data registries.
- C. Consensus opinion of experts was the primary source of recommendation.

Classes of Recommendations:

I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful and effective

II: Conditions for which there is conflict of evidence and/or a divergence of opinion about usefulness/efficacy of procedure or treatment

IIa: Weight of evidence/opinion is in favour by evidence/efficacy

IIb: Usefulness/efficacy is less well established by evidence/opinion

III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful



## CLINICAL ALGORITHM(S)

Algorithms are provided for the treatment and goals of control for patients with coronary heart disease or coronary heart disease equivalents, and for patients without coronary heart disease or coronary heart disease risk equivalents.

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

These guidelines provide recommendations that were adapted from other international guidelines on lipids and modified to suit the local situation. International guidelines used as references include the 2001 U.S. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel [ATP] III) (Bethesda [MD]: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung and Blood Institute; 2001; see the related National Guideline Clearinghouse summary [Third report of the National Cholesterol Education Program \(NCEP\) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults \(Adult Treatment Panel III\)](#)), the 1998 European Prevention of Coronary Heart Disease in Clinical Practice which was adapted from the previous recommendations of the Second Joint Task Force of European and other Societies on Coronary Prevention (Wood DA, De Backer G, Faergeman O, et al. Prevention of coronary heart disease in clinical practice. Recommendations of the Second Joint Task Force of the European Society for Cardiology, European Atherosclerosis Society and European Society of Hypertension. Eur Heart J 1998; 19:1434-1503) and the 1998 joint British recommendations (Joint British recommendations on prevention of coronary heart disease in clinical practice. British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, British Diabetic Association. Heart 1998; 80[Suppl 2]: S1-S29).

These recommendations are based on the best available current evidence and expert judgment. The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

- Primary and secondary prevention of coronary heart disease
- Reduction of cerebrovascular events
- Reduction of low-density lipoprotein cholesterol and triglyceride levels
- Decreased morbidity and mortality due to coronary heart disease

Subgroups Most Likely to Benefit:

Patients in high-risk groups, specifically those with pre-existing coronary heart disease, cerebrovascular disease, peripheral artery disease, or diabetes mellitus.

#### POTENTIAL HARMS

- Fibrates carry an increased risk of gallstones, myopathy, and elevation of liver enzymes (transaminases)
- There is low compliance with nicotinic acid because of the numerous side effects such as flushing of the face, itching of the skin and gastric irritation

Subgroups Most Likely to be Harmed:

In renal transplant patients who are on immunosuppressive therapy, caution must be exercised in the administration of statins because of the marked increase in risk of myopathy and even rhabdomyolysis.

### CONTRAINDICATIONS

#### CONTRAINDICATIONS

- Fibrates are contraindicated when the creatinine clearance is  $<10$  ml/min.
- Statins are contraindicated in women who are pregnant or who are likely to be pregnant.

### QUALIFYING STATEMENTS

#### QUALIFYING STATEMENTS

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of the original guideline document are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

### IMPLEMENTATION OF THE GUIDELINE

#### DESCRIPTION OF IMPLEMENTATION STRATEGY

Quality indicators for lipids management as well as performance parameters and recommended review frequency for performance are provided in the original guideline document.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness  
Staying Healthy

### IOM DOMAIN

Effectiveness  
Patient-centeredness  
Safety

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Lipids. Singapore: Singapore Ministry of Health; 2001 Jul. 52 p. [19 references]

### ADAPTATION

These guidelines provide recommendations that were adapted from other international guidelines on lipids and modified to suit the local situation. International guidelines used as references include the 2001 U.S. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel [ATP] III) (Bethesda [MD]: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung and Blood Institute; 2001; see the related [National Guideline Clearinghouse Guideline Summary](#)), the 1998 European Prevention of Coronary Heart Disease in Clinical Practice which was adapted from the previous recommendations of the Second Joint Task Force of European and other Societies on Coronary Prevention (Wood DA, De Backer G, Faergeman O, et al. Prevention of coronary heart disease in clinical practice. Recommendations of the Second Joint Task Force of the European Society for Cardiology, European Atherosclerosis Society and European Society of Hypertension. Eur Heart J 1998;19:1434-1503) and the 1998 joint British recommendations (Joint British recommendations on prevention of coronary heart disease in clinical practice. British Cardiac Society, British Hyperlipidaemia Association, British Hypertension Society, British Diabetic Association. Heart 1998;80[Suppl 2]:S1-S29).

### DATE RELEASED

2001 Jul

### GUIDELINE DEVELOPER(S)

National Committee on Cardiac Care (Singapore) - National Government Agency [Non-U.S.]  
National Medical Research Council (Singapore Ministry of Health) - National Government Agency [Non-U.S.]  
Singapore Cardiac Society - Medical Specialty Society  
Singapore Ministry of Health - National Government Agency [Non-U.S.]

#### GUIDELINE DEVELOPER COMMENT

These guidelines were developed by an expert workgroup appointed by the Joint Cardiovascular Working Committee of the Singapore Cardiac Society and the Singapore National Committee on Cardiac Care.

#### SOURCE(S) OF FUNDING

Singapore Ministry of Health

#### GUIDELINE COMMITTEE

Workgroup on Lipids

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Workgroup Members: Prof Chia Boon Lock (Chairman); Dr Tan Chee Eng (Vice-Chairman); Dr Maurice Choo; Dr Shanta Emmanuel; Assoc Prof Lau Kean Wah; Dr Lim Heok Seng; Dr Low Lip Ping; Dr Gary Ong Pang Yeow; Dr Susan Quek; Assoc Prof Sunil Sethi; Dr Charles Toh; Dr Mabel Yap; Prof Moti L Kashyap (Advisor)

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#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

#### GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

None available

#### NGC STATUS

This summary was completed by ECRI on April 16, 2002. The information was verified by the guideline developer as of April 19, 2002.

#### COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions. Please contact the Ministry of Health, Singapore by e-mail at [MOH\\_INFO@MOH.GOV.SG](mailto:MOH_INFO@MOH.GOV.SG).

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